

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

FUNKE *et al.*

Appl. No.: 10/581,348

§ 371(c) Date: April 6, 2007

For: **Active Compound Combinations
Having Insecticidal Properties**

Confirmation No.: 4992

Art Unit: 1616

Examiner: PAK, JOHN D.

Atty. Docket: 2400.0430000/RWE/PDL

Declaration of Heike Hungenberg Under 37 C.F.R. § 1.132

Commissioner for Patents
PO Box 1450
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I, Heike Hungenberg, of Grünewaldstr. 39b, 40764 Langenfeld, Germany,
a citizen of Langenfeld, Germany, hereby declare:

1. That I am a biologist, having studied at the University of Giessen, Germany.
2. I am named as an inventor in U.S. Patent Application No. 10/581,348 ("the Application").
3. I am presently employed by Bayer CropScience AG, the assignee of above-captioned application.
4. That I currently hold the position of a scientist within the group of Product and Project Support, in which I supervise the biological tests of insecticides.

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5. That I have read and understood the specification and claims of the Application.
6. That compounds I-1-1, I-1-4, I-1-12, I-1-24, I-1-52, I-1-54, ethiprole and fipronil, described in the Application, were tested as described in Examples A-D, below.
7. That Examples A-D were carried out under my supervision and control.
8. That the expected efficacy of a given combination of two compounds is calculated as follows (see Colby, S.R., "Calculating Synergistic and antagonistic Responses of Herbicide Combinations," *Weeds* 15:20-22, 1967):

If

X is the efficacy expressed in % mortality of the untreated control for test compound A at a concentration of m ppm respectively m g/ha,

Y is the efficacy expressed in % mortality of the untreated control for test compound B at a concentration of n ppm respectively n g/ha,

E is the efficacy expressed in % mortality of the untreated control using the mixture of A and B at m and n ppm respectively m and n g/ha,

then is
$$E = X + Y - \frac{X * Y}{100}$$

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If the observed insecticidal efficacy of the combination is higher than the one calculated as "E," then the combination of the two compounds is more than additive, i.e., there is a synergistic effect.

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Appl. No. 10/581,3489. Example A: *Myzus persicae* -- test

Solvent: 78 parts by weight of acetone
1.5 parts by weight of dimethylformamide

Emulsifier: 0.5 parts by weight of alkylaryl polyglycoether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amount of solvent and emulsifier, and the concentrate is diluted with emulsifier-containing water to the desired concentration.

Cabbage leaves (*Brassica oleracea*) which are heavily infested by the green peach aphid (*Myzus persicae*) are treated by being sprayed with the preparation of the active compound at the desired concentration.

After the specified period of time, the mortality in % is determined. 100 % means that all the aphids have been killed; 0 % means that none of the aphids have been killed.

According to the present application, in this test, *e.g.*, the following combinations listed in Tables A1 and A2 show synergistic effects in comparison to the single compounds:

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FUNKE *et al.*
Appl. No. 10/581,348Table A1
Plant damaging insects**Myzus persicae – Test**

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 1^d</u>
I-1-4	4	0
Ethiprole	4	0
I-1-4 + Ethiprole (1:1) according to the invention	4 + 4	obs.* cal.** 40 0

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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Plant damaging insects

Myzus persicae – Test

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 6^d</u>
I-1-54	4 0.8	80 20
I-1-1	4 0.8 0.16	90 60 0
I-1-24	4	0
I-1-12	4 0.8	70 40
Ethiprole	4 0.8	0 0
Fipronil	0.16	0
I-1-54 + Ethiprole (1:1) according to the invention	4 + 4	<u>obs.*</u> <u>cal.**</u> 100 80
I-1-24 + Ethiprole (1:1) according to the invention	4 + 4	<u>obs.*</u> <u>cal.**</u> 60 0
I-1-12 + Ethiprole (1:1) according to the invention	0.8 + 0.8	<u>obs.*</u> <u>cal.**</u> 60 40
I-1-1 + Fipronil (1:1) according to the invention	0.16 + 0.16	<u>obs.*</u> <u>cal.**</u> 20 0

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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Appl. No. 10/581,34810. Example B: *Phaedon cochleariae* – test

Solvent: 78 parts by weight of acetone
1.5 parts by weight of dimethylformamide

Emulsifier: 0.5 parts by weight of alkylaryl polyglycolether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amount of solvent and emulsifier, and the concentrate is diluted with emulsifier-containing water to the desired concentration.

Cabbage leaves (*Brassica oleracea*) are treated by being sprayed with the preparation of the active compound at the desired concentration and are infested with larvae of the mustard beetle (*Phaedon cochleariae*) as long as the leaves are still moist.

After the specified period of time, the mortality in % is determined. 100 % means that all the beetle larvae have been killed; 0 % means that none of the beetle larvae have been killed.

According to the present application, in this test, e.g., the following combinations listed in Tables B1 and B2 show synergistic effects in comparison to the single compounds:

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Table B1

Plant damaging insects
Phaedon cochleariae – test

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 2^d</u>
I-1-52	0.16	33
	0.032	0
I-1-1	4	67
	0.8	50
I-1-24	4	50
	0.8	17
I-1-12	0.8	33
	0.16	0
I-1-4	4	67
	0.8	33
Ethiprole	0.8	50
Fipronil	0.8	83
	0.16	33
I-1-24 + Ethiprole (1:1)		<u>obs.*</u> <u>cal.**</u>
according to the invention	0.8 + 0.8	83 58.5
I-1-12 + Ethiprole (1:1)		<u>obs.*</u> <u>cal.**</u>
according to the invention	0.8 + 0.8	100 66.5
I-1-4 + Ethiprole (1:1)		<u>obs.*</u> <u>cal.**</u>
according to the invention	0.8 + 0.8	100 66.5

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I-1-S2 + Fipronil (1:1) according to the invention	0.16 + 0.16	<u>obs.*</u> 100	<u>cal.**</u> 55.11
I-1-1 + Fipronil (1:1) according to the invention	0.8 + 0.8	<u>obs.*</u> 100	<u>cal.**</u> 91.5
I-1-24 + Fipronil (1:1) according to the invention	0.8 + 0.8	<u>obs.*</u> 100	<u>cal.**</u> 85.89
I-1-12 + Fipronil (1:1) according to the invention	0.16 + 0.16	<u>obs.*</u> 83	<u>cal.**</u> 33

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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Table B2

Plant damaging insects
Phaedon cochleariae – test

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 6^d</u>
I-1-54	0.16	67
I-1-52	0.8	83
	0.16	33
I-1-1	0.8	50
	0.032	0
I-1-12	0.8	33
	0.16	0
I-1-4	0.8	33
	0.16	0
Ethiprole	0.8	67
	0.16	33
Fipronil	0.16	50
I-1-54 + Ethiprole (1:1)	0.16 + 0.16	<u>obs.*</u> <u>cal.**</u>
according to the invention		100 77.89
I-1-52 + Ethiprole (1:1)	0.16 + 0.16	<u>obs.*</u> <u>cal.**</u>
according to the invention		83 55.11
I-1-1 + Ethiprole (1:1)	0.8 + 0.8	<u>obs.*</u> <u>cal.**</u>
according to the invention		100 83.5

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I-1-12 + Fipronil (1:1)		<u>obs.*</u>	<u>cal.**</u>
according to the invention	0.16 + 0.16	83	50
I-1-4 + Fipronil (1:1)		<u>obs.*</u>	<u>cal.**</u>
according to the invention	0.16 + 0.16	67	50

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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Appl. No. 10/581,34811. Example C: *Spodoptera frugiperda* – test

Solvent: 78 parts by weight of acetone
1.5 parts by weight of dimethylformamide

Emulsifier: 0.5 parts by weight of alkylaryl polyglycoether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amount of solvent and emulsifier, and the concentrate is diluted with emulsifier-containing water to the desired concentration.

Cabbage leaves (*Brassica oleracea*) are treated by being sprayed with the preparation of the active compound at the desired concentration and are infested with larvae of the fall army worm (*Spodoptera frugiperda*) as long as the leaves are still moist.

After the specified period of time, the mortality in % is determined. 100 % means that all the caterpillars have been killed; 0 % means that none of the caterpillars have been killed.

According to the present application, in this test, e.g., the following combinations listed in Tables C1 and C2 show synergistic effects in comparison to the single compounds:

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Table C1

Plant damaging insects
Spodoptera frugiperda -- test

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 2^d</u>
I-1-54	0.8	67
	0.16	50
	0.032	0
I-1-4	0.8	50
Ethiprole	0.8	0
Fipronil	0.16	17
I-1-54 + Ethiprole (1:1)		<u>obs.*</u> <u>cal.**</u>
0.8 + 0.8		83 67
according to the invention		
I-1-4 + Ethiprole (1:1)		<u>obs.*</u> <u>cal.**</u>
0.8 + 0.8		83 50
according to the invention		
I-1-54 + Fipronil (1:1)		<u>obs.*</u> <u>cal.**</u>
0.16 + 0.16		100 58.5
according to the invention		

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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Table C2

Plant damaging insects
Spodoptera frugiperda – test

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 6^d</u>
I-1-52	0.16 0.032	83 50
I-1-24	0.032	50
I-1-12	0.032	67
Ethiprole	0.032	0
Fipronil	0.16	17
I-1-52 + Ethiprole (1:1) according to the invention	0.032 + 0.032	<u>obs.*</u> <u>cal.**</u> 100 50
I-1-24 + Ethiprole (1:1) according to the invention	0.032 + 0.032	<u>obs.*</u> <u>cal.**</u> 100 50
I-1-12 + Ethiprole (1:1) according to the invention	0.032 + 0.032	<u>obs.*</u> <u>cal.**</u> 100 67
I-1-52 + Fipronil (1:1) according to the invention	0.16 + 0.16	<u>obs.*</u> <u>cal.**</u> 100 85.89
I-1-12 + Fipronil (1:1) according to the invention	0.032 + 0.032	<u>obs.*</u> <u>cal.**</u> 100 72.61

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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Appl. No. 10/581,34812. Example D: **Tetranychus** test (OP-resistant/dip test)

Solvent: 78 parts by weight of acetone
1.5 parts by weight of dimethylformamide

Emulsifier: 0.5 parts by weight of alkylaryl polyglykoether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amount of solvent and emulsifier, and the concentrate is diluted with emulsifier-containing water to the desired concentration.

Bean plants (*Phaseolus vulgaris*) which are heavily infested with all stages of the two-spotted spider mite (*Tetranychus urticae*) are treated by being sprayed with the preparation of the active compound at the desired concentration.

After the specified period of time, mortality in % is determined. 100 % means that all the spider mites have been killed; 0 % means that none of the spider mites have been killed.

According to the present application, in this test, e.g., the following combination listed in Table D1 shows a synergistic effect in comparison to the single compounds:

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Appl. No. 10/581,348Table D1
Plant damaging mites**Tetranychus urticae (OP-resistant) - Test**

<u>Active Ingredient</u>	<u>Concentration</u> <u>in g/ha</u>	<u>Efficacy</u> <u>in % after 6st</u>
I-1-24	4	0
	0.16	0
Ethiprole	4	0
I-1-24 + Ethiprole (1:1)		<u>obs.*</u> <u>cal.**</u>
according to the invention	4 + 4	50 0

* obs. = observed insecticidal efficacy

** cal. = efficacy calculated with Colby-formula

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13. The undersigned declarant declares further that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed at Monheim, Germany,

1.6.2011
Date

Heike H. B.
NAME

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